Acute phase protein concentrations in dogs with nasal disease

Papers

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The concentrations of C-reactive protein (CRP), serum amyloid A, haptoglobin (Hp) and α_1-acid glycoprotein were measured in dogs with clinical signs of nasal disease and compared with those of healthy dogs in order to determine the expression of these proteins in cases of canine nasal disease. A significant difference (P<0.001) between the symptomatic group and the control group was found for both CRP and Hp. Among the animals with nasal disease, a significant intergroup difference (P<0.05) was found in the expression of Hp between dogs with aspergillosis and those with chronic rhinitis.

ACUTE PHASE proteins (APPs) are serum proteins whose concentrations change as part of an innate host defence mechanism called the acute phase response. The acute phase response to inflammation protects the host from disease and injury, minimises tissue damage and enhances the rate of repair (Eckersall 2000). The acute phase response is stimulated by the release of proinflammatory cytokines including interleukin-1, tumour necrosis factor-α and interleukin-6 from monocytes and macrophages in response to tissue damage or infection (Dinarello 1984, Heinrich and others 1990). Positive APPs, which include C-reactive protein (CRP), serum amyloid A (SAA), haptoglobin (Hp), α_1-acid glycoprotein (AGP) and caeruloplasmin, all show increased plasma concentrations after tissue injury, whereas both albumin and transferrin decrease in concentration and are described as negative APPs. Both CRP and SAA are considered to be major APPs because their concentrations in plasma are characterised by an early sharp rise followed by a rapid decline. Hp and AGP are moderate APPs: they show more gradual increases of smaller magnitude, and then return to normal reference levels.

CRP, the first APP to be discovered, has a molecular weight of 100 kDa. Higher mortalities have been associated with elevations in plasma concentrations of CRP in cases of aortic aneurysm in human beings (Schillinger and others 2002). CRP has also been shown to be a sensitive and inexpensive marker of inflammation for the early diagnosis of bacterial infection after orthopaedic surgery in human beings (Waleczek and others 1991). In dogs, CRP has been shown to be elevated in various disorders, including pancreatitis, pyometra, pneumonia, immune-mediated haemolytic anaemia and postsurgical trauma (Yamamoto and others 1993, 1994, Fransson and others 2004, Holm and others 2004, Couto and others 2009, Mitchell and others 2009). A decrease in the level of CRP has also been shown to be correlated with survival in dogs with systemic inflammatory response syndrome or sepsis (Gebhardt and others 2009).

SAA is a small serum protein with a molecular weight of 11,685 Da. It is produced by hepatocytes and is a non-specific marker of infectious, inflammatory, immunological and traumatic disease (Eckersall 1995). The plasma concentrations of SAA have been shown to increase more rapidly compared with other APPs; in dogs, horses and human beings the plasma concentrations may increase 100- to 1000-fold in response to acute inflammation (Pepys and others 1989, Eckersall and others 1999a, Glojnaric and others 2001).

Hp is a glycoprotein that is synthesised in the liver. Its primary role is in the complexing of free haemoglobin after intravascular haemolysis. Serum concentrations of Hp decrease in cases of haemolytic disease and increase in response to inflammatory disease (Mischke and others 2007).

Canine AGP, as in other species, is a protein with an unusually high proportion of glycosyl groups (45 per cent) contributing to its molecular weight of 43 kDa. Changes in glycosylation of AGP have been described in human beings and also in cats with feline infectious peritonitis (Ceciliani and others 2004).

Canine nasal disease is a common clinical entity seen in small animal practice, which can arise due to neoplasia, foreign bodies, inflammation, bacterial, mycotic or parasitic infections and dental disease (Tasker and others 1999, Meler and others 2008). The aetiology of nasal disease in dogs remains a diagnostic challenge, and a definitive diagnosis cannot be made from clinical findings alone. Diagnosis of

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TABLE 1: Median and range of serum acute phase protein concentrations in groups of dogs with nasal disease and healthy dogs

	C-reactive protein (mg/l)		Haptoglobin (g/l)		α_1-acid glycoprotein (g/l)		Serum amyloid A (mg/l)	
Disease group	Median (n)	Range	Median (n)	Range	Median (n)	Range	Median (n)	Range
Aspergillosis	13.4** (13)	2-82	5.2**† (13)	2.0-19.2	0.38 (10)	0.23-0.88	0.63 (10)	<0.12-64
Rhinitis	4.8** (17)	1-44	2.9** (17)	0.8-5.8	0.42 (16)	0.17-2.4	0.41 (16)	0.13-5.5
Neoplasia	14.8** (18)	<0.78-69	4.1** (18)	0.30-10.8	0.42 (18)	0.27-3.7	0.82* (18)	0.22-35.7
Healthy dogs	1.5 (51)	<0.78-9.6	0.65 (54)	<0.02-4.3	0.42 (37)	0.24-0.77	0.49 (39)	<0.12-8.8

* Significantly different from the healthy group (P<0.05), ** Significantly different from the healthy group (P<0.001)
† Significantly different from the rhinitis group P<0.01

canine nasal disease usually requires a combination of investigative techniques including radiography, CT, MRI, rhinoscopy, bacteriology, mycology and cytological or histological examination of nasal samples collected at the time of investigation. A recent retrospective study showed that a definitive diagnosis could not be established in 36.3 per cent of cases of canine nasal disease (Meler and others 2008).

The purpose of this study was to determine whether serum concentrations of APPs alter in clinical cases of canine nasal disease, and to investigate whether there is a significant variation in plasma APP concentrations among the different phenotypic groups diagnosed.

Materials and methods

Client-owned dogs presented to the authors' institutions between September 2007 and September 2009 with a history of persistent nasal disease were considered eligible for inclusion in the study. All the cases received a full clinical examination with specific emphasis on nasal examination. This included examination of the external nares for evidence of discharge and the nature of the discharge, if any; examining for evidence of nasal planum ulceration or depigmentation; visual examination and palpation for the presence of facial asymmetry and/or pain; assessment of nasal patency; and palpation of regional lymph nodes for evidence of enlargement.

Blood samples were collected at the time of presentation and before any invasive procedures, for routine haematology, biochemistry and aspergillosis serology tests and an APP panel. The panel of APPs run for this study was measured on residual samples taken for a primary clinical purpose, which would have otherwise been discarded as clinical waste. The panel comprised CRP, SAA, AGPt and Hp. Serum samples taken for analysis of the APPs were stored at –20°C until assayed. The concentrations of the APPs were determined as described previously by Lowrie and others (2009a, b). The CRP immunoturbidimetric assay and Hp haemoglobin binding capacity assays have been described earlier by Eckersall and others (1991, 1999b). SAA was measured using a commercial canine ELISA kit (Tridelta Development), and AGP was measured using a commercial radial immunodiffusion assay (J-Path) in accordance with the manufacturer's instructions. The limit of detection of the CRP immunoassay, based on 2 sd from blank samples with zero or negligible amounts of CRP, was 0.78 mg/l, and had interassay coefficients of variation (CVs) (n=20) of 24 and 24 per cent with control samples of 39 and 140 mg/l, respectively. For SAA, the limit of detection was 0.12 mg/l with interassay CVs (n=9) of 31 and 12 per cent with control samples of 9.3 and 50 mg/l, respectively. Although these CVs were higher than for clinical chemistry analytes, they were considered acceptable for immunoassay because they were all less than the recommended 25 per cent (Findlay and others 2000) except for SAA at a low concentration (9.3 mg/l, CV=31 per cent). However, given that the serum concentration of this analyte in dogs can rise to over 2000 mg/l (Lowrie and others 2009b) and given the large dynamic range, this higher CV was also considered acceptable. The limit of detection of the Hp assay was 0.02 g/l and interassay CVs (n=18) were 5 and 7 per cent with control samples of 0.3 and 1.0 g/l, respectively. The limit of detection of the AGP assay was 0.02 g/l and a control sample concentration of 0.43 g/l (n=3) had an interassay CV of 2.7 per cent.

The serum APP concentration results from the dogs with nasal disease were compared with those from dogs (irrespective of breed, age or sex) that were free from inflammatory or infectious disease. Serum samples previously described by Mischke and others (2007) were included in the control samples for this study. However, not all samples from healthy dogs from the laboratory's serum bank were available for all APP assays. The sera were assayed for concentrations of CRP (n=51), Hp (n=54), AGP (n=37) and SAA (n=39), using the methods described above.

Diagnostic imaging procedures were performed for all dogs under sedation or general anaesthesia. These included radiography of the nasal cavities (right or left lateral, intraoral dorsoventral and rostrocaudal view of frontal sinus), CT or MRI.

The nasopharynx and choanae of all the dogs were examined with a retroflexed endoscope using an 8.5 mm flexible videoendoscope (Olympus) for evidence of loss of symmetry, inflammation, foreign bodies or masses. The pharynx was packed with gauze swabs and a 30° 9.5 Fr (including sheath) rigid cystoscope (Karl Storz) with a sterile saline flushing channel was used for anterograde rhinoscopy. The dorsal and ventral meatus were inspected for evidence of neoplasia, fungal plaques, turbinate destruction and foreign bodies. Biopsy samples collected during endoscopic examination were submitted for histopathological examination and bacterial and fungal culture.

The dogs were assigned to one of three groups – neoplasia, aspergillosis or chronic rhinitis – based on the diagnostic imaging findings, positive results for either fungal culture or aspergillosis serology and the results of the histological analysis.

The data were explored graphically and statistical comparisons of APP levels among groups (control, aspergillosis, rhinitis and neoplasia) were carried out using Kruskal-Wallis tests. Mann-Whitney U tests were used for post hoc pairwise comparisons. Significance was set at $P<0.05$, and multiple comparisons were accounted for using a Bonferroni correction. All analyses were undertaken in R (R Development Core Team 2009).

Dogs were excluded from the study if they had received steroid treatment in the seven days before APP sampling, because steroid treatment is known to stimulate the production of Hp in dogs (Martínez-Subiela and others 2004, Cerón and others 2005).

This study was approved by the welfare and ethics committee of the University of Glasgow.

Results

Forty-eight dogs with nasal disease were included in the study. The animals were assigned to one of three groups depending on their diagnosis: neoplasia (n=18), aspergillosis (n=13) and rhinitis (n=17). The mean (sd) age of the animals in the study was 7.79 (2.82) years (range 0.5 to 12 years). The breeds included cocker spaniel (n=5), golden retriever (n=5), Border collie (n=3), Staffordshire bull terrier (n=3), German shepherd dog (n=3), rottweiler (n=3), West Highland white terrier (n=2), Jack Russell terrier (n=2), springer spaniel (n=2), lurcher (n=2), Cavalier King Charles spaniel (n=2), samoyed (n=2) and one each of the following: German pointer, bull mastiff, boxer, labrador retriever, briard, English bulldog, greyhound and German visla. There were also six crossbreed dogs.

The median and range of CRP concentrations in the three groups of dogs with nasal disease are given in Table 1 and shown in Fig 1, along with the concentrations found in healthy dogs (Mishke and others 2007). Post hoc comparisons revealed that serum samples from each of the three groups of dogs with nasal disease had elevated CRP concentrations compared with the samples from healthy animals ($P<0.001$ for each group relative to controls). However, there were no significant differences in CRP levels among the groups with different nasal diseases.

The median and range of Hp concentrations in the three groups of dogs with nasal disease are given in Table 1 and shown in Fig 2, along with the concentrations found in healthy dogs. Again, post hoc comparisons identified the differences between the serum samples from each of the diseased groups and the samples from healthy animals to be statistically significant ($P<0.001$ for each group relative to con-

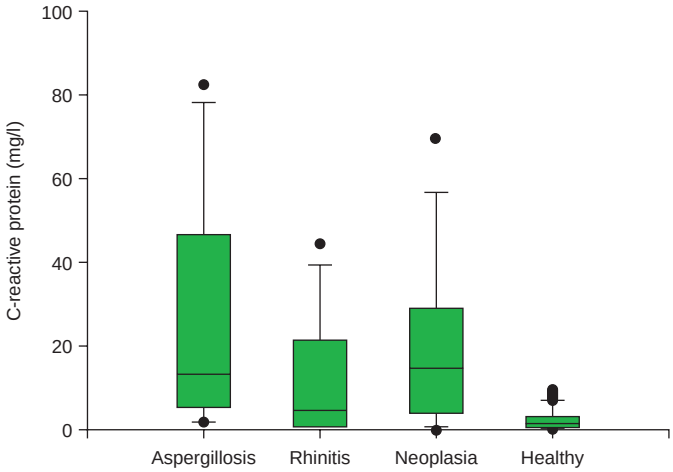

FIG 1: Serum concentrations of C-reactive protein in dogs with aspergillosis (n=13), rhinitis (n=17) and neoplasia (n=18) compared with those of healthy dogs (n=51)

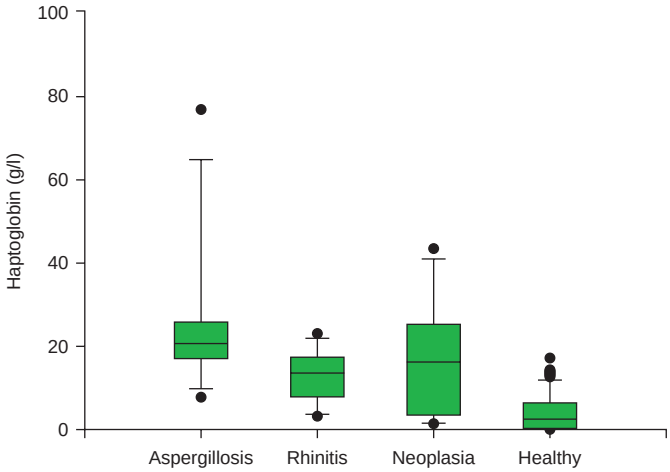

FIG 2: Serum concentrations of haptoglobin in dogs with aspergillosis (n=13), rhinitis (n=17) and neoplasia (n=18) compared with those of healthy dogs (n=54)

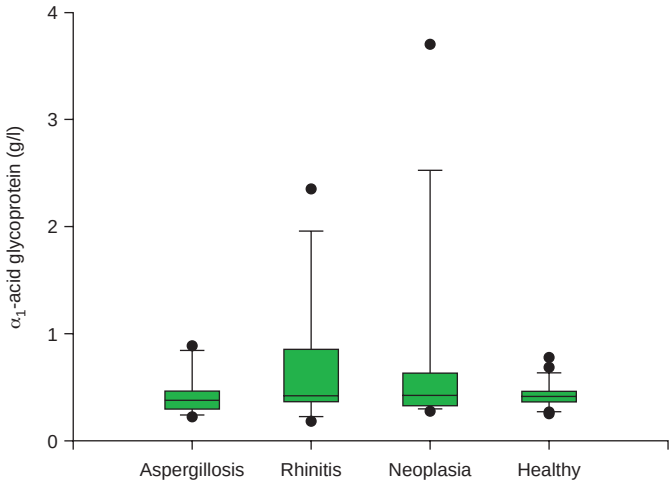

FIG 3: Serum concentrations of α_1-acid glycoprotein in dogs with aspergillosis (n=10), rhinitis (n=16) and neoplasia (n=18) compared with those in healthy dogs (n=37)

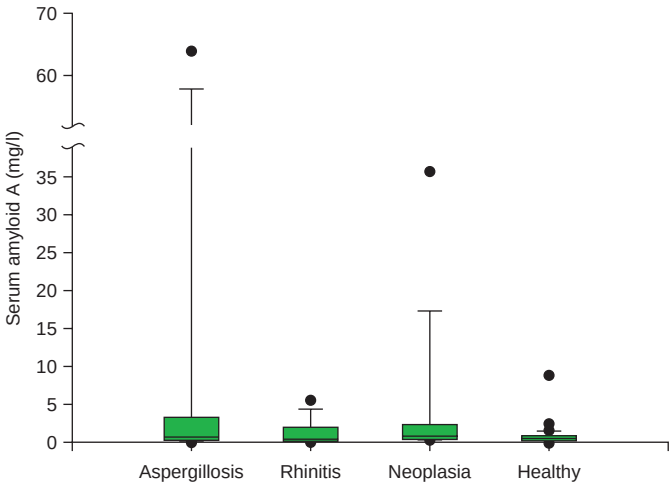

FIG 4: Serum concentrations of serum amyloid A in dogs with aspergillosis (n=10), rhinitis (n=16) and neoplasia (n=18) compared with those in healthy dogs (n=39)

trols). The median Hp concentration in the aspergillosis group (5.2 g/l) was also found to be significantly different ($P<0.01$) from the median concentration in the rhinitis group (2.9 g/l).

The median and range of AGP concentrations in the three groups of dogs with nasal disease are given in Table 1 and shown in Fig 3, along with the concentrations found in healthy dogs. There were no significant differences among the groups ($P=0.612$) as determined by non-parametric analysis of variance (Kruskal-Wallis test), irrespective of whether the samples from the healthy group were included in the analysis.

The median and range of SAA concentrations in the three groups of dogs with nasal disease are given in Table 1 and shown in Fig 4, along with the concentrations found in healthy dogs. A significant difference ($P<0.05$) was found between the neoplasia group and the control group.

Discussion

APPs are widely used as non-specific markers of inflammation in dogs (Eckersall 2000, Cerón and others 2005). Recent publications have shown that APPs aid in the diagnosis of certain conditions and are of prognostic value (Conner and others 1988, Holm and others 2004, Gebhardt and others 2009). APPs have also been shown to be elevated in normal physiological conditions such as pregnancy (Ulutas and others 2009). Recent studies in children have shown that CRP is downregulated in allergic rhinitis (Steiner and others 2006).

Canine SAA and CRP have been shown to be the major APPs in dogs (Cerón and others 2005). Changes in CRP and SAA have been shown to occur in pathological conditions such as sepsis (Gebhardt and others 2009), steroid-responsive meningitis-arteritis (SRMA) (Lowrie and others 2009a), and in bitches with pyometra being monitored for postoperative complications (Dabrowski and others 2009).

In the present study, CRP levels were found to be significantly higher in dogs with nasal disease (irrespective of the type of nasal disease) compared with controls ($P<0.001$). This was an expected finding, on the basis of results from earlier studies evaluating CRP in dogs with other inflammatory, infectious and neoplastic diseases (Burton and others 1994, Mischke and others 2007, Planellas and others 2009). The results of the SAA analysis show a significant difference between the neoplasia group ($P<0.05$) and the control group ($P<0.05$), but not between the aspergillosis group or chronic rhinitis group and the control group. The explanation for the significantly higher relative levels of CRP but not of SAA in the aspergillosis and rhinitis groups compared with the controls is not clear. The findings suggest, however, that the mechanisms that control these major APPs in dogs are different from those in human beings (Cerón and others 2005). It is possible that SAA production is stimulated only under certain conditions or at particular levels of pathogenesis. The results of the present study contrast with those of a study that investigated the APP response to SRMA (Lowrie and others 2009a). It is evident that SRMA caused the stimulation of both APPs, possibly due to differences in the locations of the lesions or to the severity of the inflammatory process. Further investigation is warranted to determine the explanation for this finding, and to interpret the differential elevations

of these APPs under different conditions with a view to improving the accuracy of diagnosis.

Hp and AGP are APPs that show moderate elevation in levels during acute phase reactions (Cerón and others 2005). The concentrations of Hp and AGP have been shown to increase in many infectious and inflammatory conditions, including surgical trauma (Conner and others 1988), SRMA (Lowrie and others 2009a) and lymphatic neoplasia (Mischke and others 2007). Significant differences in Hp concentrations ($P<0.001$) were found between the groups of animals with nasal disease and the control group, but no differences were found in the mean AGP concentrations among the groups. In addition, a significant difference ($P<0.01$) was detected between the serum concentrations of Hp in the aspergillosis group and the chronic rhinitis group. Of the moderate APPs in dogs, Hp has been found to be more responsive than AGP in other conditions such as SRMA. A significant increase in serum Hp concentration has also been shown after administration of different dosages of exogenous glucocorticoids (Cerón and others 2005). The samples for the present study were taken at least seven days after any steroid treatment and therefore the significant increases in Hp concentration found here were not likely to be due to an iatrogenic effect (Martínez-Subiela and others 2004). A more valid explanation would be that Hp shows a greater response to the on-going nature of the inflammatory response in these diseases than AGP does. Recently, the role of APPs in monitoring disease progression has been shown to have some validity (Gebhardt and others 2009, Lowrie and others 2009b).

Canine aspergillosis is a common clinical entity. Effective control of the disease has often been difficult to achieve, and a wide variety of treatment modalities has been investigated, including topical and systemic administration of antifungal agents or combinations of the two routes of administration (Sissener and others 2006, Peeters and Clercx 2007). Affected dogs are often left with a chronic nasal discharge due to turbinate destruction, which can make the decision to terminate treatment difficult. The significant difference in the expression of Hp in dogs with aspergillosis and those with chronic rhinitis provides a basis to examine cases after treatment in order to determine whether resolution of the APP rise is confined only to cases in which the outcome of treatment is a success. This knowledge may be useful in the therapeutic management of aspergillosis cases and in differentiating active aspergillosis from chronic rhinitis.

A number of outliers were identified. A 12-year-old dog that was diagnosed with nasal aspergillosis had a depressed skull fracture and an organising haematoma. Another outlier was an 11-year-old rottweiller with a nasal sarcoma and severe osteoarthritis. This finding is interesting, given that marked elevations in one or more of the APP markers may prompt the clinician to look for concurrent or underlying pathology that may be of clinical significance when treating cases of nasal disease.

The limitations of this study include the small number of cases in the individual groups and the retrospective nature of the analysis. The median value of CRP was elevated in both the neoplasia (14.8 mg/l) and aspergillosis (13.4 mg/l) groups compared with the chronic rhinitis (4.8 mg/l) group, although no significant inter-group difference was found. Future studies with larger numbers of cases in each group may show significant inter-group differences. This study has shown that CRP and Hp are useful biomarkers to detect nasal inflammation. Whether the concentrations of APPs in dogs with rhinitis can be used as prognostic factors or to monitor the development of the disease has to be investigated in further studies.

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Conflict of interest

PDE is a director and shareholder of ReactivLab; LB is an employee of ReactivLab.

References

BURTON, S. A., HONOR, D. J., MACKENZIE, A. L., ECKERSALL, P. D., MARKHAM, R. J. & HORNEY, B. S. (1994) C-reactive protein concentration in dogs with inflammatory leukograms. *American Journal of Veterinary Research* **55**, 613-618

CECILIANI, F., GROSSI, C., GIORDANO, A., POCACQUA, V. & PALTRINIERI, S. (2004) Decreased sialylation of the acute phase protein alpha$_1$-acid glycoprotein in feline infectious peritonitis (FIP). *Veterinary Immunology and Immunopathology* **99**, 229-236

CERÓN, J. J., ECKERSALL, P. D. & MARTÍNEZ-SUBIELA, S. (2005) Acute phase proteins in dogs and cats: current knowledge and future perspectives. *Veterinary Clinical Pathology* **34**, 85-99

CONNER, J. G., ECKERSALL, P. D., FERGUSON, J. & DOUGLAS, T. A. (1988) Acute phase response in the dog following surgical trauma. *Research in Veterinary Science* **45**, 107-110

COUTO, C. G., CERÓN, J. J., PARRA, M. D., MARTÍNEZ-SUBIELA, S. & LAZBIK, M. C. (2009) Acute phase protein concentrations in retired racing greyhounds. *Veterinary Clinical Pathology* **38**, 219-223

DABROWSKI, R., KOSTRO, K., LISIECKA, U., SZCZUBIAL, M. & KRAKOWSKI, L. (2009) Usefulness of C-reactive protein, serum amyloid A component, and haptoglobin determinations in bitches with pyometra for monitoring early post-ovariohysterectomy complications. *Theriogenology* **72**, 471-476

DINARELLO, C. A. (1984) Interleukin-1 and the pathogenesis of the acute-phase response. *New England Journal of Medicine* **311**, 1413-1418

ECKERSALL, P. D. (1995) Acute phase proteins as markers of inflammatory lesions. *Comparative Haematology International* **5**, 93-97

ECKERSALL, P. D. (2000) Recent advances and future prospects for the use of acute phase proteins as markers of disease in animals. *Revue de Médicine Vétérinaire* **151**, 577-584

ECKERSALL, P. D., BENNETT, D., MCCOMB, C., WEBER, A. & MCDONALD, T. (1999a) The acute phase response in dogs with arthritis. Proceedings of the 4th European Comparative Clinical Pathology Meeting. Verona, June 1 to 4, 1999

ECKERSALL, P. D., CONNER, J. G. & HARVIE, J. (1991) An immunoturbidimetric assay for canine C-reactive protein. *Veterinary Research Communications* **15**, 17-24

ECKERSALL, P. D., DUTHIE, S., SAFI, S., MOFFATT, D., HORADAGODA, N. U., DOYLE, S., PARTON, R., BENNETT, D. & FITZPATRICK J. L. (1999b) An automated biochemical assay for haptoglobin: prevention of interference from albumin. *Comparative Haematology International* **9**, 117-124

FINDLAY, J. W., SMITH, W. C., LEE, J. W., NORDBLOM, G. D., DAS, I., DESILVA, B. S., KHAN, M. N. & BOWSHER, R. R. (2000) Validation of immunoassays for bioanalysis: a pharmaceutical industry perspective. *Journal of Pharmaceutical and Biomedical Analysis* **21**, 1249-1273

FRANSSON, B. A., KARLSTAM, E., BERGSTROM, A., LAGERSTEDT, A. S., PARK, J. S., EVANS, M. A. & RAGLE, C. A. (2004) C-reactive protein in the differentiation of pyometra from cystic endometrial hyperplasia/mucometra in dogs. *Journal of the American Animal Hospital Association* **40**, 391-399

GEBHARDT, C., HIRSCHBERGER, J., RAU, S., ARNDT, G., KRAINER, K., SCHWEIGERT, F. J., BRUNNBERG, L., KASPERS, B. & KOHN, B. (2009) Use of C-reactive protein to predict outcome in dogs with systemic inflammatory response syndrome or sepsis. *Journal of Veterinary Emergency and Critical Care* **19**, 450-458

GLOJNARIC, I., CASL, M. T., SIMIC, D. & LUKAC, J. (2001) Serum amyloid A protein (SAA) in colorectal carcinoma. *Clinical Chemistry and Laboratory Medicine* **39**, 129-133

HEINRICH, P. C., CASTELL, J. V. & ANDUS, T. (1990) Interleukin-6 and the acute phase response. *Biochemical Journal* **265**, 621-636

HOLM, J. L., ROZANSKI, E. A., FREEMAN, L. M. & WEBSTER, C. R. L. (2004) C-reactive protein concentrations in canine acute pancreatitis. *Journal of Veterinary Emergency and Critical Care* **14**, 183-186

LOWRIE, M., PENDERIS, J., ECKERSALL, P. D., MCLAUGHLIN, M., MELLOR, D. & ANDERSON, T. J. (2009a) The role of acute phase proteins in diagnosis and management of steroid-responsive meningitis arteritis in dogs. *Veterinary Journal* **182**, 125-130

LOWRIE, M., PENDERIS, J., MCLAUGHLIN, M., ECKERSALL, P. D. & ANDERSON, T. J. (2009b) Steroid responsive meningitis-arteritis: a prospective study of potential disease markers, prednisolone treatment, and long-term outcome in 20 dogs (2006-2008). *Journal of Veterinary Internal Medicine* **23**, 862-870

MARTÍNEZ-SUBIELA, S., GINEL, P. J. & CERÓN, J. J. (2004) Effects of different glucocorticoid treatments on serum acute phase proteins in dogs. *Veterinary Record* **154**, 814-817

MELER, E., DUNN, M. & LECUYER, M. (2008) A retrospective study of canine persistent nasal disease: 80 cases (1998-2003). *Canadian Veterinary Journal* **49**, 71-76

MISCHKE, R., WATERSTON, M. & ECKERSALL, P. D. (2007) Changes in C-reactive protein and haptoglobin in dogs with lymphatic neoplasia. *Veterinary Journal* **174**, 188-192

MITCHELL, K. D., KRUTH, S. A., WOOD, R. D. & JEFFERSON, B. (2009) Serum acute phase protein concentrations in dogs with autoimmune hemolytic anemia. *Journal of Veterinary Internal Medicine* **23**, 585-591

PEETERS, D. & CLERCX, C. (2007) Update on canine sinonasal aspergillosis. *Veterinary Clinics of North America. Small Animal Practice* **37**, 901-916

PEPYS, M. B., BALTZ, M. L., TENNENT, G. A., KENT, J., OUSEY, J. & ROSSDALE, P. D. (1989) Serum amyloid A protein (SAA) in horses: objective measurement of the acute phase response. *Equine Veterinary Journal* **21**, 106-109

PLANELLAS, M., BASSOLS, A., SIRACUSA, C., SACO, Y., GIMÉNEZ, M., PATO, R. & PASTOR, J. (2009) Evaluation of serum haptoglobin and C-reactive protein in dogs with mammary tumors. *Veterinary Clinical Pathology* **38**, 348-352

R DEVELOPMENT CORE TEAM (2009). R: a Language and Environment for Statistical Computing. R Foundation for Statistical Computing

SCHILLINGER, M., DOMANOVITS, H., BAYEGAN, K., HÖLZENBEIN, T., GRABENWÖGER, M., THOENISSEN, J., RÖGGLA, M. & MÜLLNER, M. (2002) C-reactive protein and mortality in patients with acute aortic disease. *Intensive Care*

Medicine **28**, 740-745
SISSENER, T. R., BACON, N. J., FRIEND, E., ANDERSON, D. M. & WHITE, R. A. (2006) Combined clotrimazole irrigation and depot therapy for canine nasal aspergillosis. *Journal of Small Animal Practice* **47**, 312-315
STEINER, I., SOBIESKA, M., PUCHER, B., GRZEGOROWSKI, M. & SAMBORSKI, W. (2006) Examination of acute phase proteins concentrations in children with allergic rhinitis. *Annales Academiae Medicae Stetinensis* **52**, 33-37 (In Polish)
TASKER, S., KNOTTENBELT, C. M., MUNRO, E. A., STONEHEWER, J., SIMPSON, J. W. & MACKIN, A. J. (1999) Aetiology and diagnosis of persistent nasal disease in the dog: a retrospective study of 42 cases. *Journal of Small Animal Practice* **40**, 473-478
ULUTAS, P. A., MUSAL, B., KIRAL, F. & BILDIK, A. (2009) Acute phase protein levels in pregnancy and oestrus cycle in bitches. *Research in Veterinary Science* **86**, 373-376
WALECZEK, H., KOZIANKA, J. & EVERTS, H. (1991) C-reactive protein in the early diagnosis of postoperative infection following bone surgery. *Der Chirurg* **62**, 866-870 (In German)
YAMAMOTO, S., SHIDA, T., MIYAJI, S., SANTSUKA, H., FUJISE, H., MUKAWA, K., FURUKAWA, E., NAGAE, T. & NAIKI, M. (1993) Changes in serum C-reactive protein levels in dogs with various disorders and surgical traumas. *Veterinary Research Communications* **17**, 85-93
YAMAMOTO, S., SHIDA, T., OKIMURA, T., OTABE, K., HONDA, M., ASHIDA, Y., FURUKAWA, E., SARIKAPUTI, M. & NAIKI, M. (1994) Determination of C-reactive protein in serum and plasma from healthy dogs and dogs with pneumonia by ELISA and slide reversed passive latex agglutination test. *Veterinary Quarterly* **16**, 74-77

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